UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,327	04/12/2001	Samuel J. Danishefsky	2003080-0081(SK-719-Z)	3477

24280 7590 10/06/2004

Choate, Hall & Stewart
Exchange Place
53 State Street
Boston, MA 02109

EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,327	DANISHEFSKY ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *108,110-114 and 116-119* is/are pending in the application.

4a) Of the above claim(s) *112 and 113* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *108,110,111,114 and 116-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 108, 110, 114 and 116 have been amended. Claim 115 has been canceled. Claims 108, 110-114, 116-119 are pending. Claims 112 and 113 remain withdrawn from consideration. Claims 108, 110, 111, 114, 116-119 are under consideration.

2. Sections of Title 35, US Code, not found in this action can be found in a previous action.

3. The rejections of claims 110 and 116 under 35 U.S.C. 102(b) as being anticipated by Nudelman et al (The Journal of Biological Chemistry, 1986, Vol. 261, pp. 11247-11253, cited in a previous Office action) or Windmuller et al (Tetrahedron Letters, 1994, Vol. 35, pp. 7927-7930, cited in a previous Office action) is maintained for reasons of record. a

Claims 110 and 116 are drawn in part to the recited chemical structure, wherein r, m and n are independently 0, 1, 2 or 3; and where R is substituted or unsubstituted allyl. The specific embodiments of "wherein R is a ceramide moiety, the set of indices (r, m, n) is not (1, 0 and 1)" have been canceled in response to the new matter rejection of the previous Office action.

Nudelman et al teach the chemical structure of claims 110 and 116 wherein R is ceramide and the indices are r=1, m=0 and n=1 (Structure 2 of abstract).

Windmuller et al teach the chemical structure of claims 110 and 116 wherein R is ceramide or an Sp linking group of (CH2)8CO2Me (page 7929, figure 2c).

4. Applicant argues that the instant references do not anticipate the claims because neither reference discloses a linker consisting of a succinimide or the specified structure. This has been considered but not found persuasive. The claim is drawn to the illustrated structure wherein R is H, substituted or non-substituted allyl, Windmuller et al disclose the linker as ceramide which comprises an unsubstituted allyl group. In the case of R=H, substituted or unsubstituted allyl, the claim does not require a carrier group. The carrier group is required only for the moiety having the structure of –LINKER-CROSSLINKERq-CARRIER-. Therefore applicant is arguing limitations which are not in claims 110 and 116.

5. The rejection of claims 108, 110, 111, 114 and 116-119 under 35 U.S.C. 103 (a) as being unpatentable over Etlinger (EP 429,816) in view of Sytokowski (WO 95/25746) and Nudleman et al (Journal of Biological Chemistry, 1986, Vol. 261, pp. 11247-11253) and Kaizu et al (Journal of Biological Chemistry, 1986, vol. 281, pp. 11254-11258, cited in a previous Office action) is maintained for reasons of record.

Claims 110 and 116 are drawn to the recited chemical structure, wherein r, m and n are independently 0, 1, 2 or 3; and where R is substituted or unsubstituted allyl, an amino acyl moiety, or a moiety having the structure of a linker-(crosslinker)q-carrier, wherein the linker is an alky of allyl group having between 1 and 9 carbons, and wherein the crosslinker is selected from the group consisting of succinimide and the recited cyclohexane hydrizide structure; claim 116 is further characterizes the claimed product as a composition comprising the described chemical structure, which further comprises and immunological adjuvant, or pharmaceutically acceptable carrier.

Claims 108 and 114 are drawn to the recited trifucosyl chemical structure , wherein said structure is bound to a suitable carrier protein or peptide, said structure being bound either directly or indirectly by a crosslinker selected from the group consisting of succinimide and a linker having a recited cyclohexane hydrizide structure; claim 114 further characterizes the claimed product as a composition comprising the described chemical structure, which further comprises and immunological adjuvant, or pharmaceutically acceptable carrier.

Claim 117 embodies the compositions of claims 114 and 116 wherein the carrier protein is BSA, polylysine of KLH.

Claim 118 embodies the compositions of claims 114 and 116 wherein the immunological adjuvant is bacteria or liposomes. Claim 119 embodies the composition of claim 118 wherein the adjuvant is S. minnesota, BCG or QS21.

Etlinger teaches a method for inducing a humoral response comprising the administration of an antigen which comprises a B-cell epitope linked to a carrier protein., wherein the carrier protein comprises a T-helper cell epitope (page 2, lines 22-25, page 3, lines 39-49, page 4, lines 23-34). Etlinger teaches the administration of the composition with adjuvant (page 8, lines 14-32). Etlinger does not teach the B-cell epitope having the recited trifucosyl chemical structure, although Etlinger et al suggest a broader scope fro the claimed method (page 8, lines 53-55)

Sytoloski teaches that for glycoproteins, a heterobifunctional cross linking reagent can be attached to a carbohydrate moiety and linked to a primary amine within a peptide (page 7, lines 17-28). Sytoloski teaches that 4-(N-maleimidomethyl) cycloheaxane-1-carboxyl-hydrazide can be used as a linking reagent (page 15, lines 20-25), fulfilling the specific embodiments of claims 108, 110, 114 and 116 drawn to the linking structure.

Nudelman et al teach the structure of the trifucononasylceramide as structure 2. Nudelman et al teach that said glycolipid antigen is a major component of LeY-active components detected in human colonic carcinoma cases (page 11250, second column, line 24 under "Discussion" to page 11251, first column, line 8). Nudleman et al teach that the expression of the LeY antigen as diagnostic and prognostic value (page 11250, second column, lines 16-17 under "Discussion"). Nudelman et al teach that the addition of the third Fucosyl group (structure 2 versus structure 1 of abstract) provides antigenicity for the glycolipid (page 11251, first column, last sentence).

Kaizu et al teach that administration of the trifucononasylceramide to mice with Salmonella minnesota as adjuvant produced the IgM KH1 antibody with a novel specificity for trifucononasylceramide (page 11256, first column, lines 1-5 under :Discussion"), thus fulfilling the specific embodiments of claims 118 and 119, drawn to the administration of the composition with an immunological adjuvant of S minnesota. Kaizu et al teach that only the trifucononasylceramide was able to inhibit the biding of the KH1 antibody to trifucononasylceramide (page 11255, first column, paragraph entitled "specificity of antibody KH1"). Kaizu et al teach that the KH1 antibody shows higher specificity for human colon adenocarcinoma than do other LeY antibodies that react promiscuously with all carbohydrate chains containing LeY.

Windmuller et al teach the chemical synthesis of the claimed trifucosyl structure by the linking of "building blocks". Windmuller et al teach the synthesis of building block 5 with the spacer of (CH2)8CO2Me which would allow for the attachment of the carrier protein linked by the reagent 4-(N-maleimidomethyl) cycloheaxane-1-carboxyl-hydrazide as taught by Sytoloski.

It would have been *prima facie o*bvious at the time the claimed invention was made to use the trifucononasylceramide structure identified by Kaizu as the B-cell epitope in the method taught by Etlinger and attach said trifucononasylceramide to the carrier protein or peptide by the

linker protein taught by Sytoloski. One of skill in the art would have been motivated to do so through the teachings of Kaizu et al on the antigenic structure of the trifucononasylceramide which elicits the IgM antibody which binds to colonic adenocarcinoma tissue and the teachings of Sytoloski on the use of bifunctional linker proteins such as to link primary amines of proteins with a carbohydrate in glycoproteins and the teachings of Windmuller on the chemical synthesis of building block 5 having the spacer of (CH2)8CO2Me. One of skill in the art would be motivated to use the teachings of Etlinger to produce a stronger humoral immune response in the mice injected with the trifucononasylceramide in order to obtain a high titer antibody.

6. Applicant argues that Etlinger does not teach B-cell, epitopes having the claimed carbohydrate epitope. Applicant is reminded that if Etlinger did indeed teach the instant epitope the rejection would have been made under 102 rather than 103. Applicant argues that there are no teachings or suggestions in Sytokowski of carbohydrate constructs useful fro the treatment of cancer of for the eliciting of antibodies that bind to tumor cells. this has been considered but not found persuasive. Sytokowski was relied upon for the teaching of heterobifunctional cross-linking reagents which are used to link a carbohydrate to a peptide , not for the motivation to combine the references. In fact, Kaizu et al teach that the KH1 antibody, which binds to the disclosed epitope, shows higher specificity for human colon adenocarcinoma and Nudelman et al teach the structure of the trifucononasylceramide as structure 2. Nudelman et al teach that the claimed epitope is a major component of LeY-active components detected in human colonic carcinoma cases (page 11250, second column, line 24 under "Discussion" to page 11251, first column, line 8). Nudleman et al teach that the expression of the LeY antigen as diagnostic and prognostic value (page 11250, second column, lines 16-17 under "Discussion"). Nudelman et al teach that the addition of the third Fucosyl group (structure 2 versus structure 1 of abstract) provides antigenicity for the glycolipid (page 11251, first column, last sentence). Thus, Kaizu et al and Nudleman et al provide motivation to one of skill in the art to make antibodies to the claimed epitope. Sytokowski provides the enablement for heterobifunctional linkers useful for attaching carbohydrate groups to proteins. Etlinger provides the motivation to attach a T-helper cell epitope by means of the heterobifunctional linker. One of skill in the art would be motivated to make the carbohydrate epitope disclosed by Kaizu et al and Nudleman et al linked to a T-cell

helper epitope in order to have a stronger humoral immune response against the carbohydrate epitope. One of skill in the art would know that a heterobifunctional linking group as disclosed by Sytokowski et al would provide for the attachment of the carbohydrate epitope on one end and the T-helper cell epitope on the other.

7. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
10/4/2004

Karen A Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER